

What is claimed is:

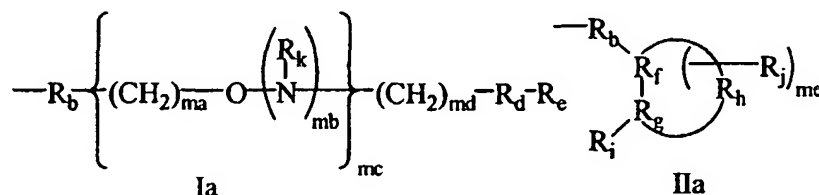
1. A composition comprising a first oligomeric compound and a second oligomeric compound, wherein:
 - 5 at least a portion of said first oligomeric compound is capable of hybridizing with at least a portion of said second oligomeric compound,
at least a portion of said first oligomeric compound is complementary to and capable of hybridizing to a selected target nucleic acid,
one of said first and said second oligomeric compounds comprises a plurality of
10 linked nucleosides linked by internucleoside linking groups, and
the other one of said first and said second oligomeric compounds comprises a plurality of linked nucleosides linked by internucleoside linking groups and wherein essentially each of said nucleosides is other than 2'-OH and have 3'-endo conformational geometry;
 - 15 wherein said first and second oligomeric compounds optionally comprise at least one phosphate group, a 5' or 3'-overhang or a conjugate group.
2. The composition of claim 1 wherein said first oligomeric compound comprises a plurality of linked nucleosides linked by internucleoside linking groups and wherein
20 essentially each of said nucleosides is other than 2'-OH and have 3'-endo conformational geometry.
3. The composition of claim 1 wherein said second oligomeric compound comprises a plurality of linked nucleosides linked by internucleoside linking groups and wherein
25 essentially each of said nucleosides is other than 2'-OH and have 3'-endo conformational geometry.
4. The composition of claim 1 wherein each of said nucleosides of said first oligomeric compound comprise a β -D-ribofuranose sugar group.
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5. The composition of claim 1 wherein each of said nucleosides of said second oligomeric compound comprise a β -D-ribofuranose sugar group.

6. The composition of claim 1 wherein the 3'-terminus of said first oligomeric compound comprises a stabilizing or conjugate group.
7. The composition of claim 6 wherein said stabilizing group is a capping group or a dTdT dimer.
8. The composition of claim 6 wherein the 3'-terminus of said first oligomeric compound comprises a conjugate group.
9. The composition of claim 1 wherein said first oligomeric compound comprises a 5'-phosphate group.
10. The composition of claim 1 wherein the 5'-terminus of said first oligomeric compound comprises a stabilizing or conjugate group.
11. The composition of claim 10 wherein said stabilizing group is a capping group.
12. The composition of claim 10 wherein the 5'-terminus of said first oligomeric compound comprises a conjugate group.
13. The composition of claim 1 wherein said second oligomeric compound has a 5'-phosphate group.
14. The composition of claim 1 wherein each of said internucleoside linking groups of said first oligomeric compound is, independently, a phosphodiester or a phosphorothioate.
15. The composition of claim 14 wherein each of said internucleoside linking groups of said first oligomeric compound is a phosphodiester.
16. The composition of claim 14 wherein each of said internucleoside linking groups of said first oligomeric compound is a phosphorothioate.

17. The composition of claim 1 wherein each of said internucleoside linking groups of said second oligomeric compound is, independently, a phosphodiester or a phosphorothioate.
- 5 18. The composition of claim 17 wherein each of said internucleoside linking groups of said second oligomeric compound is a phosphodiester.
19. The composition of claim 17 wherein each of said internucleoside linking groups of said second oligomeric compound is a phosphorothioate.
- 10 20. The composition of claim 1 wherein the 3'-terminus of said second oligomeric compound comprises a stabilizing or conjugate group.
21. The composition of claim 20 wherein said stabilizing group is a capping group or
15 a dTdT dimer.
22. The composition of claim 20 wherein the 3'-terminus of said second oligomeric compound comprises a conjugate group.
- 20 23. The composition of claim 1 wherein the 5'-terminus of said second oligomeric compound comprises a stabilizing or conjugate group.
24. The composition of claim 23 wherein said stabilizing group is a capping group.
- 25 25. The composition of claim 23 wherein the 5'-terminus of said second oligomeric compound comprises a conjugate group.
26. The composition of claim 2 wherein each of said nucleosides of said second oligomeric compound has 3'-endo conformational geometry.
- 30 27. The composition of claim 3 wherein each of said nucleosides of said first oligomeric compound has 3'-endo conformational geometry.

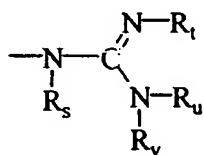
28. The composition of claim 1 wherein each of said nucleoside having 3'-endo conformational geometry comprises a 2'-substituent group.

29. The composition of claim 28 wherein each of said 2'-substituent groups is, independently, -F, -O-CH₂CH₂-O-CH₃, -O-CH₃, -O-CH₂-CH=CH₂ or a group having one of formula I_a or II_a:



wherein:

- 10 R_b is O, S or NH;
 R_d is a single bond, O, S or C(=O);
 R_e is C₁-C₁₀ alkyl, N(R_k)(R_m), N(R_k)(R_n), N=C(R_p)(R_q), N=C(R_p)(R_r) or has formula III_a;



- 15 III_a
- R_p and R_q are each independently hydrogen or C₁-C₁₀ alkyl;
 R_r is -R_x-R_y;
 each R_s, R_t, R_u and R_v is, independently, hydrogen, C(O)R_w, substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl, substituted or unsubstituted C₂-C₁₀ alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group or a conjugate group, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl;
 or optionally, R_u and R_v, together form a phthalimido moiety with the nitrogen atom to which they are attached;
 25 each R_w is, independently, substituted or unsubstituted C₁-C₁₀ alkyl, trifluoromethyl, cyanoethyloxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-

fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl or aryl;

R_k is hydrogen, a nitrogen protecting group or $-R_x-R_y$;

R_p is hydrogen, a nitrogen protecting group or $-R_x-R_y$;

5 R_x is a bond or a linking moiety;

R_y is a chemical functional group, a conjugate group or a solid support medium;

each R_m and R_n is, independently, H, a nitrogen protecting group, substituted or unsubstituted C_1-C_{10} alkyl, substituted or unsubstituted C_2-C_{10} alkenyl, substituted or unsubstituted C_2-C_{10} alkynyl, wherein the substituent groups are selected from hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, alkynyl; NH_3^+ , $N(R_u)(R_v)$, guanidino and acyl where said acyl is an acid amide or an ester;

or R_m and R_n , together, are a nitrogen protecting group, are joined in a ring structure that optionally includes an additional heteroatom selected from N and O or are
15 a chemical functional group;

R_i is OR_z , SR_z , or $N(R_z)_2$;

each R_z is, independently, H, C_1-C_8 alkyl, C_1-C_8 haloalkyl, $C(=NH)N(H)R_u$, $C(=O)N(H)R_u$ or $OC(=O)N(H)R_u$;

R_f , R_g and R_h comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms wherein said heteroatoms are selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

R_j is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, $N(R_k)(R_m)$ OR_k , halo, SR_k or CN;

m_a is 1 to about 10;

each m_b is, independently, 0 or 1;

m_c is 0 or an integer from 1 to 10;

30 m_d is an integer from 1 to 10;

m_e is from 0, 1 or 2; and

provided that when m_c is 0, m_d is greater than 1.

30. The composition of claim 28 wherein each of said 2'-substituent groups is, independently, -F, -O-CH₂CH₂-O-CH₃, -O-CH₃, -O-CH₂-CH=CH₂ or -O-CH₂-CH-CH₂-NH(R_j) where R_j is H or C₁-C₁₀ alkyl.
- 5 31. The composition of claim 28 wherein each of said 2'-substituent groups is, independently, -F, -O-CH₂CH₂-O-CH₃ or -O-CH₃.
32. The composition of claim 31 wherein each of said 2'-substituent groups is -O-CH₃.
- 10 33. The composition of claim 32 wherein each of said internucleoside linking groups of said first oligomeric compound is a phosphodiester.
34. The composition of claim 33 wherein each of said internucleoside linking groups of said second oligomeric compound is a phosphodiester.
- 15 35. The composition of claim 33 wherein each of said internucleoside linking groups of said second oligomeric compound is a phosphorothioate.
- 20 36. The composition of claim 28 wherein each of said internucleoside linking groups of said first oligomeric compound is a phosphorothioate.
37. The composition of claim 36 wherein each of said internucleoside linking groups of said second oligomeric compound is a phosphodiester.
- 25 38. The composition of claim 36 wherein each of said internucleoside linking groups of said second oligomeric compound is a phosphorothioate.
39. The composition of claim 1 wherein said first and said second oligomeric compounds are a complementary pair of siRNA oligonucleotides.
- 30 40. The composition of claim 39 wherein said first and said second oligomeric compounds have 3'-dTdT overhangs.

41. The composition of claim 39 wherein said first and said second oligomeric compounds have blunt ends.
42. The oligomeric compound of claim 1 further comprising at least one terminal cap moiety.
43. The oligomeric compound of claim 42 wherein said terminal cap moiety is attached to one or both of the 3'-terminal and 5'-terminal ends of said oligomeric compound.
44. The oligomeric compound of claim 43 wherein said terminal cap moiety is an inverted deoxy abasic moiety.
45. The composition of claim 1 wherein said first and said second oligomeric compounds are an antisense/sense pair of oligonucleotides.
46. The composition of claim 1 wherein each of said first and second oligomeric compounds has from about 8 to about 80 nucleobases.
47. The composition of claim 1 wherein each of said first and second oligomeric compounds has from about 10 to about 50 nucleobases.
48. The composition of claim 1 wherein each of said first and second oligomeric compounds has from about 12 to about 30 nucleobases.
49. The composition of claim 1 wherein each of said first and second oligomeric compounds has from about 12 to about 24 nucleobases.
50. The composition of claim 1 wherein each of said first and second oligomeric compounds has from about 19 to about 23 nucleobases.
51. The composition of claim 1 wherein said first oligomeric compound is an antisense oligonucleotide.

52. The composition of claim 51 wherein said second oligomeric compound is a sense oligonucleotide.

53. A method of inhibiting gene expression comprising contacting one or more cells,
5 a tissue or an animal with a composition of claim 1.